



Management of acute pancreatitis in children

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Purpose of review

Pediatric acute pancreatitis has been on the rise in the last decades, with an incidence close to adult pancreatitis. In the majority of cases acute pancreatitis resolves spontaneously, but in a subset of children the disease progresses to severe acute pancreatitis with attendant morbidity and mortality.

Recent findings

Pediatric acute pancreatitis in this era is recognized as a separate entity from adult acute pancreatitis given that the causes and disease outcomes are different. There are slow but important advances made in understanding the best management for acute pancreatitis in children from medical, interventional, and surgical aspects.

Summary

Supportive care with fluids, pain medications, and nutrition remain the mainstay for acute pancreatitis management. For complicated or severe pancreatitis, specialized interventions may be required with endoscopic or drainage procedures. Surgery has an important but limited role in pediatric acute pancreatitis.

Keywords

children, interventions, medical management, pancreatitis

INTRODUCTION

In recent years, there has been an increasing incidence of pediatric acute pancreatitis and has reached a current estimate of 1/10000 cases. Increased awareness may be one factor contributing to this trend [1]. Management of pediatric acute pancreatitis remains challenging given the lack of guidelines and the sparse literature on the outcomes associated with different regimens [2]. Previously published adult guidelines do not apply directly to children [3], since children are not 'mini adults' and causes for pediatric acute pancreatitis vary greatly from adult acute pancreatitis [2]. To overcome some of the challenges with acute pancreatitis management in children, we are providing an updated summary of advances made in this field in each of the following areas: medical, interventional, and surgical. The aim of this document is to serve as a quick reference for clinicians managing acute pancreatitis in children.

DIAGNOSIS AND MEDICAL MANAGEMENT

Diagnosis of acute pancreatitis requires the presence of two out of three criteria from the following: symptoms: abdominal pain consisting of pancreatic origin or vomiting, laboratory findings of amylase and/or lipase at or above three times upper limit of normal,

radiologic findings supportive of acute pancreatitis by imaging [4]. The symptoms of acute pancreatitis presentation may vary by patient age as the signs and symptoms can be more subtle and nonspecific in toddlers relative to older age groups [5]. This makes the diagnosis of acute pancreatitis challenging in pediatrics, and more so management in certain situations difficult, given the absence of consensus pediatric guidelines for acute pancreatitis management. For imaging abdominal ultrasound is one of the most common modalities used in the work up of acute pancreatitis; it is capable of diagnosing gallstone pancreatitis and can identify findings supportive of acute pancreatitis on presentation. Computed tomography and MRI is most often reserved for complicated acute pancreatitis as these imaging studies possess a greater sensitivity for the detection of pancreatic necrosis or other disease complications [2].

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KEY POINTS

- Acute pancreatitis incidence in pediatrics is estimated to be at 1/10 000 cases.
- Aggressive fluid management is associated with improved outcomes in pediatric acute pancreatitis.
- Early nutrition is associated with improved outcomes in pediatric acute pancreatitis.
- Severe acute pancreatitis carries the risk of increased morbidity in about one third of cases of acute pancreatitis.
- ERCP is most often reserved for therapeutic interventions.
- Surgical interventions are indicated only when medical and endoscopic interventions have failed or are not feasible in cases of acute pancreatitis and in specific anatomic circumstances.

Most pediatric acute pancreatitis cases resolve spontaneously without complication, but in a subset of patients up to 34% can progress to severe acute pancreatitis with attendant morbidity, and rarely mortality [6]. Most recently, disease severity of acute pancreatitis in pediatrics has been classified by a group of expert pancreatologists in pediatric as well as adult pancreatology into mild, moderate, and severe [7[■]]. This new classification is not only important in providing a common definition for acute pancreatitis severity, but moreover would allow for the development of management algorithms in the future based on risk-stratified patient populations, and outcome studies in pediatric acute pancreatitis. Mild acute pancreatitis is the most common form of pediatric acute pancreatitis and usually resolves spontaneously with supportive measures. Moderately severe acute pancreatitis is associated with transient organ failure of less than 48 h duration, or development of local pancreatic complications (fluid collections, necrosis, and hemorrhage). Severe acute pancreatitis is a serious risk for prolonged morbidity and/or mortality and is associated with organ dysfunction lasting longer than 48 h [7[■]]. Children in the moderately severe or the severe categories benefit from the care provided by specialized pediatric centers with pancreatic expertise in gastroenterology, advanced endoscopy, surgery as well as intensive care monitoring. Having a prognostic system or tool to predict severe acute pancreatitis on admission is needed to help risk stratify the patients early on in the course of the disease [6], before complications arise.

Medical management of acute pancreatitis consists mainly of supportive care with intravenous (i.v.)

fluid resuscitation, pain control, and nutrition management. Although there are few studies that have evaluated the feasibility of allowing early nutrition and the role of i.v. fluid management in pediatric acute pancreatitis, they are mostly designed for mild acute pancreatitis cases [8,9[■]]. With the limited nature of these studies, the practice in pediatrics has advanced toward early aggressive fluid resuscitation on admission for the first 24 h, defined as an i.v. fluid administration rate of 1.5–2 times the maintenance rate. In addition, early implementation of enteral nutrition, oral versus using existing feeding tubes, has been integrated into the management algorithms with favorable outcomes [9[■]]. Despite the advances that have been made in the management of mild and moderately severe acute pancreatitis, our knowledge on how best to care for those with severe pancreatitis significantly lags behind, as we lack the evidence-based guidelines for optimal fluid management and timing of nutrition initiation.

Adequate pain management is needed in most cases of acute pancreatitis and requires a careful balance between adequate control and oversedation. There are no data on optimal pain management in pediatric acute pancreatitis and studies in adults have not identified a single superior medication. For mild to moderate pain, opioid-sparing medications have been used, including indomethacin, and other non-steroidal anti-inflammatory medications as well as acetaminophen. Opioids are reserved for severe pain and include morphine or hydromorphone, as well as other opiates with data reassuring against sphincter of Oddi spasm as had previously been believed. In terms of medication usage in acute pancreatitis management, previous studies have not found a superior effect of one particular medication in altering the course of the disease. These studies included an evaluation of steroids, empiric antibiotic use (in the absence of infected necrosis), supplemental pancreatic enzymes, protein C, enteral supplementation, and others [2]. Antibiotic use in acute pancreatitis is reserved for cases of infected pancreatic necrosis.

ENDOSCOPY AND INTERVENTIONAL MANAGEMENT

In most cases, there is a selective role of endoscopic intervention in the management of acute pancreatitis in children. The specific cause behind the development of acute pancreatitis significantly directs the algorithm between medical management with supportive care versus endoscopic intervention. Over the last several years, the integration of endoscopic retrograde cholangiopancreatography (ERCP) in the care of children with pancreatic and biliary disorders has expanded [10–13]. A handful of studies have

focused on the application of ERCP specific to pancreatitis and pancreatic disorders [14–16]. The latest endoscopic technological innovation to impact the care of children is endoscopic ultrasound (EUS) [17,18].

Role of endoscopic retrograde cholangiopancreatography in acute pancreatitis

Numerous ERCP case series of pediatric-aged patients have recently emerged, with reports of their safety and efficacy when implemented for various pancreaticobiliary disorders. Of the encountered causes in which ERCP may be beneficial, biliary indications (including biliary pancreatitis) continue to be the most common [19]. Biliary pancreatitis most commonly results from migration of a gallstone or sludge from the gallbladder into the common bile duct resulting in pancreatic duct/drainage obstruction [20], whereas in others, the presence of an anomalous pancreaticobiliary junction with reflux of bile into the pancreatic duct or the propensity of sludge or debris to accumulate within a dilated long common channel can be a secondary process for the development of acute pancreatitis [21]. Irrespective of the mechanistic process, persistent obstructive stone or sludge as a cause of acute pancreatitis often warrants ERCP intervention.

Acute pancreatitis may also be a result of blunt abdominal trauma with pancreatic injury that may or may not involve the main pancreatic duct. In such situations, ERCP may be of diagnostic benefit to determine the degree of injury severity, but may also be therapeutic by means of a temporary pancreatic duct stent to resolve a ductal leak and in other cases by restoring ductal continuity [22–24]. Though optimal management strategies of blunt pancreatic trauma continue to be of significant debate, recent studies including one from a large population trauma registry and another from a multinstitutional collaborative group have taken steps toward addressing the controversy [25,26].

Of key importance to recognize when weighing the benefits versus the risks from ERCP intervention, is the risk of inducing or exacerbating pancreatitis by performance of the procedure itself. A recent meta-analysis for the purpose of identifying complication rates from ERCP performed in children found a post-ERCP pancreatitis (PEP) rate of 4.7% [19]. This review included ERCP studies irrespective of procedure indication, both biliary and pancreatic. When other investigators assessed factors associated with PEP, they identified a higher rate of 10.9%, wherein pancreatic duct injection and pancreatic sphincterotomy were positively associated risk factors [27].

The major conclusion from these studies is that the risk of developing PEP in children is variable and likely dependent upon distinct patient risk factors as well as the specific intervention(s) performed.

Role of endoscopic ultrasound in acute pancreatitis

This past year saw a number of publications adding to the expanding fund of knowledge in the application of EUS to pancreaticobiliary disease in children. Recent studies from investigators reporting their use of EUS in children have shown its diagnostic and therapeutic utility for such indications as biliary obstruction (as a cause for gallstone pancreatitis), pancreatic cysts, acute/chronic pancreatitis, pancreatic mass and pancreatic trauma [17,18]. In some clinical scenarios, the findings by EUS obviated the need for ERCP [17]. An additional small case series of six procedures (performed in five patients, age range 6–17 years) from Jia *et al.* [28] demonstrated the safety and efficacy in children who underwent an EUS for indications that included celiac plexus block, pseudocyst drainage via cystgastrostomy and fine needle aspiration with cyst aspiration for diagnostic purposes. The use of endoscopic transluminal necrosectomy for management of walled-off pancreatic necrosis (WOPN) has been steadily evolving as standard of care in the adult population, but reports of its use in children have been limited until the last several years. Trikudanathan *et al.* [29] described the first pediatric case series of necrotizing pancreatitis treated successfully by endoscopic transluminal drainage and necrosectomy. More recently, the use of fully covered self-expanding metal stents in the EUS-guided drainage of WOPN has been shown to be well tolerated and efficacious in the pediatric population [30].

Figure 1 demonstrates a computed tomography scan from a patient with acute pancreatitis and WOPN.

No doubt there is much further needed investigation to be conducted to attain a greater understanding of the most appropriate EUS applications in children including the relative safety profile of therapeutic interventions. This will necessitate combined efforts amongst pediatric and adult gastroenterologists to report their collective experience including clinical outcomes.

SURGICAL MANAGEMENT

In the majority of cases of acute pancreatitis in children, medical management is successful in achieving resolution of disease. However, surgical intervention may be indicated in a subset of patients



FIGURE 1. Walled off pancreatic necrosis. Coronal image from a computed tomography scan performed with intravenous contrast in a patient with acute pancreatitis complicated by a walled off pancreatic and peripancreatic necrosis. The collection has a well defined, enhancing wall surrounding a heterogeneous fluid collection, with small foci of debris contained within the collection. Duct dilation is visible in the pancreatic head and uncinate.

when complications from acute pancreatitis occur, such as in cases of severe acute pancreatitis that have resulted in a prolonged and complicated course, including the presence of necrosis or pseudocysts. Owing to the rarity of complicated acute pancreatitis in children, surgical management is often based on adult treatment algorithms. In addition, surgery plays a role in cases of biliary pancreatitis and may be considered in some cases of traumatic pancreatic injury with main pancreatic ductal disruption.

The development of necrotizing pancreatitis confers substantial morbidity and mortality, and may require consideration for surgical intervention in the context of local complications, including infected necrosis and pseudocysts. Because evidence-based guidelines for the management of severe acute pancreatitis are lacking in children, adult treatment paradigms have typically been applied [3]. Challenges arise regarding the determination of whether pancreatic necrosis is sterile or infected, and the use of fine needle aspiration has been established as a reliable approach to identify infected necrosis in patients with clinical or radiological suspicion [31]. The gold standard for management of infected necrosis has historically been open necrosectomy [32]. However, a randomized controlled trial in adults has demonstrated the benefit of a step-up approach (percutaneous or endoscopic drainage of infected fluid, followed by minimally invasive video-assisted retroperitoneal necrosectomy) for management of infected pancreatic



FIGURE 2. Pancreatic pseudocyst. Coronal image from a computed tomography scan performed with intravenous contrast in a patient with acute pancreatitis complicated by a pancreatic pseudocyst. A well defined fluid collection with thin enhancing wall arises from the pancreatic tail. The contents of the collection are homogeneous.

necrosis with reduced complications and mortality compared to open necrosectomy [33].

Although endoscopic approaches to management of pancreatic necrosis in children provide the advantage of avoiding traditional open necrosectomy, such procedures should be limited to experienced endoscopists within the construct of a multidisciplinary team to ensure appropriate patient selection and optimal outcomes, with surgical approaches being a back-up option for failed interventions.

Pancreatic pseudocysts (encapsulated collections of pancreatic fluid) may complicate the course of severe acute pancreatitis, and usually evolve beyond 4 weeks after the onset of acute pancreatitis, Figure 2. Although most pseudocysts will resolve without intervention, if symptoms persist, local complications occur, or infection is suspected, percutaneous, endoscopic, or surgical drainage options are considered. Historically, operative approaches for symptomatic pseudocysts were standard of care, including open cystgastrostomy and cystjejunostomy. Surgical approaches have evolved with increased use of minimally invasive techniques, including demonstration of the safety and efficacy of laparoscopic cystgastrostomies in the pediatric population [34]. More recently, randomized controlled studies in adults have reported the superiority of endoscopic EUS-guided drainage of pancreatic pseudocysts compared to surgical approaches [35]. Endoscopic techniques for pseudocyst drainage have become more widespread in children as well [36], and are now a critical consideration as part of a step-up approach in the pediatric population.

Biliary pancreatitis

Surgical intervention plays a role in the management of children with biliary pancreatitis, including cases of gallstone pancreatitis and congenital anomalies of the biliary tree. In the setting of cholangitis or high index of suspicion of obstructing gallstone in the biliary system, ERCP with stone extraction should be performed expeditiously. The timing of cholecystectomy following an episode of mild gallstone pancreatitis remains debatable, however, studies report a higher frequency of biliary-related adverse events in children who undergo delayed cholecystectomy versus those who undergo operation during the index admission [37].

Choledochal cysts with associated pancreatobiliary malunion are an important cause of pancreatitis in the pediatric population [38,39]. Standard surgical management involves complete resection of the choledochal cyst with biliary reconstruction by hepaticojejunostomy [39]. Importantly, it is critical to avoid incomplete cyst excision, as remnant cystic dilation of the distal bile duct can be a cause of recurrent pancreatitis episodes postoperatively and mandates reoperation [40]. Pancreatobiliary malunion without associated choledochal cyst or common bile duct dilation is also a cause of pancreatitis in children, and recommended surgical management involves common bile duct excision with hepaticojejunostomy [41].

Traumatic pancreatic injury

Controversy remains regarding the management of traumatic pancreatic injury involving disruption of the pancreatic duct in children. Some studies have advocated nonoperative approaches to pancreatic transection in the pediatric population [42], whereas others have reported a higher association of operative management in the setting of higher grades of pancreatic injury (grade 3 or higher), particularly distal ductal injuries [25]. As already discussed, the role of ERCP in the evaluation and management of pediatric traumatic pancreatic injury continues to evolve, and consensus on its use in this setting is lacking. Recent studies in children have reported the utility of ERCP in the early diagnosis of pancreatic ductal injuries, as well as the successful definitive management of ductal disruption by endoscopic stenting [43,44]. Studies are ongoing to determine whether early distal pancreatectomy or nonoperative approaches including ERCP lead to optimal outcomes in children with high-grade traumatic pancreatic ductal injury.

CONCLUSION

Pediatric acute pancreatitis is an emerging field, not only because of increased awareness and advanced

diagnostic modalities, but more so in the work up and management of acute pancreatitis in this age group. Classification of pediatric acute pancreatitis is a new advancement made in this field that will allow risk stratification and population management directed to patient subsets to be applied. Although the majority of acute pancreatitis cases require supportive care and medical management, there remains a subset of patients that will benefit from ERCP and EUS, and less commonly, surgical interventions. Future research should include randomized prospective trials in pediatric acute pancreatitis that will lead to advanced knowledge in different fluid and nutrition management pathways and medications to halt the progression to severe acute pancreatitis. Studies are also needed to understand further the role of advanced endoscopy in pediatric acute pancreatitis. Last, we need more studies that examine the role of surgical interventions in complicated acute pancreatitis cases.

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Conflicts of interest

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- of special interest
- of outstanding interest

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